

Remarks

I. Status of the Claims

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 50-61 are pending in the application, with claim 50 being the independent claim. Claims 50, 60 and 61 are sought to be amended. Support for the amendment to claim 50 may be found in the specification, for example, at page 16, lines 23-26. Support for the amendment to claims 60 and 61 may be found in the specification, for example, at page 17, lines 3-5 and 10-16. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

II. Summary of the Office Action

In the Office Action dated July 23, 2008, the Examiner has made two rejections of the claims. Applicants respectfully offer the following remarks concerning each of these elements of the Office Action.

III. The Rejection Under 35 U.S.C. § 112, First Paragraph Is Traversed

In section 4 of the Office Action at pages 2-3, the Examiner has rejected claims 50-61 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Examiner alleges that "[t]he original claims and the original specification provide no basis" for the limitations of "greater than 90% of said uricase in tetrameric form," "at least 95% of said uricase in tertrameric [sic] form" and "at least 98% of said uricase in tertrameric [sic] form." *See* Office Action at page 2. Applicants respectfully disagree. However, in order to further prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claim 50 to remove the "greater than 90% of" language and have amended claims 60 and 61 to recite "wherein less than 5% of said uricase is in a non-tetrameric aggregated form" and "wherein less than 2% of said uricase is in a non-tetrameric aggregated form," respectively. Explicit support for the amendments to claims 60 and 61 may be found in the specification as filed at *e.g.*, page 17, lines 3-5 and 10-16. Accordingly, the claims as currently presented are fully described in the present specification. Thus, Applicants respectfully submit that the rejection of claims 50-61 for lack of written description has been overcome. Therefore, reconsideration and withdrawal are respectfully requested.

IV. The Rejection Under 35 U.S.C. § 102(b) Is Traversed

In section 5 of the Office Action at pages 4-7, the Examiner has maintained the rejection of claims 50-53 under 35 U.S.C. § 102(b) as allegedly being anticipated by Lee *et al.*, *Science* 239: 1288-1291 (1988) (hereinafter "Lee"). Applicants respectfully traverse this rejection.

First, Applicants respectfully point out that the claim construction employed by the Examiner appears to change in the middle of this rejection. Specifically, at page 5 of the Office Action, the Examiner states that "[w]e thus interpret the phrase 'wherein greater than 90% of said uricase is in a tetrameric form' as encompassing a range of

uricase above 90%, and thus any prior art uricase preparation that contains above 90% of the uricase in tetrameric form is encompassed by claim 50." *See* Office Action at page 5. However, the Examiner then goes on to state at page 6 of the Office Action that "as discussed above, claim 50 encompasses uricase preparations containing only approximately 90% of the uricase in tetrameric form." *See* Office at page 6. Hence, after stating on page 5 that claim 50 only encompasses preparations in which *more* than 90% of the uricase is tetrameric, the Examiner then states -- one page later -- that this claim only encompasses preparations in which approximately 90% of the uricase is tetrameric. Clearly, both of these mutually exclusive statements cannot be true. In fact, Applicants respectfully assert that this second claim construction is erroneous based on the claims as previously presented and *a fortiori* on the claims as currently presented. Specifically, the invention as presently claimed is directed to isolated tetrameric uricase in which "said uricase is in a substantially tetrameric form, and wherein less than 10% of said uricase is in a non-tetrameric aggregated form." Therefore, by *definition* the presently claimed tetrameric uricase preparations *must* contain greater than 90% of the uricase in the tetrameric form.

In view of this proper claim construction, Applicants again assert that Lee does not *expressly* disclose preparations of isolated tetrameric uricase in which the uricase is in a substantially tetrameric form, and wherein less than 10% is in a non-tetrameric aggregated form, as recited by the present claims. Lee only discloses three uricase preparations and *none* of these preparations is expressly disclosed as being in a substantially tetrameric form, wherein less than 10% is in a non-tetrameric aggregated form. First, Lee discloses a commercial preparation of porcine liver uricase from Sigma. Second, Lee also discloses a natural preparation of murine liver uricase. Lee does not

indicate *what* form these two uricase preparations were in, let alone that these preparations were in a substantially tetrameric form, wherein less than 10% of the uricase was in a non-tetrameric aggregated form. Moreover, as discussed in more detail below, at least the first of these preparations contains significantly more than 10% of the uricase in a non-tetrameric aggregated form. Third, Lee discloses a uricase preparation where the commercial porcine uricase and natural murine liver uricase have been "purified to homogeneity" by SDS-PAGE. *See* Lee at pages 1289 and 1291. However, the "homogeneous" uricase preparations of Lee do *not* contain 100% uricase tetramers -- instead they contain isolated monomers, formed from aggregates of isolated uricase by the SDS-PAGE process used in Lee.¹ Thus, as one of ordinary skill would readily appreciate, Lee does not expressly disclose any preparation of isolated uricase in which the uricase is in a substantially tetrameric form and less than 10% is in a non-tetrameric aggregated form.

Despite the Examiner's repeated assertions to the contrary, Applicants note that the preparations of uricase obtained by Lee for use in the preparative or analytical SDS-PAGE disclosed in that reference are not in the native tetrameric form. This fact is supported by Example 1 in the present specification which discloses that the commercial preparation of porcine liver uricase used in Lee (and also used as a starting material by the inventors of the present application) had to be purified by the methods described in the present application in order to obtain a preparation of uricase that is in a substantially tetrameric form, and wherein less than 10% of the uricase is in a non-tetrameric

¹ As one of ordinary skill would be readily aware, the use of sodium dodecylsulfate (SDS) in the polyacrylamide gel electrophoresis (PAGE) methods in Lee would result in complete disaggregation of any and every multimeric form of uricase into the monomeric subunits -- hence this method produces the

aggregated form. *See* specification at page 16, lines 23-26. The present specification further discloses that natural and recombinant uricases isolated from bacteria, fungi, mammals and plants require purification by the methods described in the present specification in order to obtain an isolated tetrameric uricase preparation in which the uricase is in a substantially tetrameric form, and wherein less than 10% of the uricase is in a non-tetrameric aggregated form. *See* specification at Examples 4-10. Thus, the commercial preparation of porcine liver uricase and the natural preparation of murine liver uricase disclosed in Lee clearly would not have been expected to contain substantially tetrameric uricase, wherein less than 10% of the uricase is in a non-tetrameric aggregated form.

This conclusion is further supported by the data presented in the Second Declaration Under 37 C.F.R. § 1.132 by Merry R. Sherman, Ph.D., filed September 18, 2007. These data clearly show that the amount of non-tetrameric aggregated uricase that is present in the commercial preparation of porcine liver uricase used both in Lee and as a starting material in Example 1 of the present application was significantly higher than the "less than 10%" required by the present claims. *See* paragraph 7 and Figure 3 of the second Sherman Declaration. As is shown in Figure 3, and as stated by Dr. Sherman at paragraph 7, the Sigma porcine liver uricase (U3250) contained 21% octamer and 17% aggregates larger than octamer prior to purification by the methods described in the present application. Furthermore, these data show that the amount of non-tetrameric aggregated uricase that is present in other isolated commercial, recombinant and natural uricase preparations was significantly higher than the "less than 10%" required by the

same result (*i.e.*, only the monomeric subunit form is observed on the gel) no matter what the state of aggregation of the uricase polypeptides applied to the gel -- tetramers, octamers, or otherwise.

present claims -- the Sigma porcine liver uricase (Catalog No. U3377) contained 11% octamer and 3% aggregates larger than octamer; the soybean uricase contained 22% octamer and 13% aggregates larger than octamer; and the *Candida utilis* uricase (Sigma Catalog No. U1878) contained 21% octamer and 19% aggregates larger than octamer, prior to purification by the methods described in the present application. *See* Figures 4 and 5 and paragraphs 8 and 10-11 of the second Sherman Declaration.

Indeed, as Dr. Sherman stated at paragraphs 10 and 16 of the second Sherman declaration and as Figures 1, 2 and 5 clearly show, preparations of uricase that contain less than 10% in a non-tetrameric aggregated form are obtainable only by using isolation methods such as those described in the present application, which are not described in Lee, thereby resulting in the presently claimed uricase preparations. *See* Figures 1, 2, and 5 and paragraphs 10 and 16 of the second Sherman Declaration. Hence, as described in the present specification, and as is clearly shown in the second Sherman Declaration, without specifically purifying the uricase preparations using methods such as those described in the present specification, the uricase preparations disclosed in Lee would not (and did not) contain substantially tetrameric uricase, wherein less than 10% of the uricase is in a non-tetrameric aggregated form. Thus, as one of ordinary skill in the art would readily appreciate, Lee does not expressly disclose an isolated tetrameric mammalian uricase having the characteristics recited in the present claims.

In addition, Applicants respectfully assert that Lee does not inherently disclose an isolated tetrameric mammalian uricase, wherein said uricase is in a substantially tetrameric form, and wherein less than 10% is in a non-tetrameric aggregated form as required by the present claims. To rely on an inherency argument, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination

that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (PTO Bd. Pat. App. Int. 1990) (emphasis in original). This burden has not been met in the present case, since there is no disclosure in Lee, nor any sound scientific reasoning, that isolated tetrameric uricase containing less than 10% non-tetrameric aggregated uricase "necessarily flow" from the disclosure in Lee.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). As discussed above, Lee does not expressly or inherently disclose every element of the presently claimed invention. Hence, under *Kalman*, this reference cannot support a rejection under 35 U.S.C. § 102(b). In view of the foregoing remarks, Applicants respectfully assert that Lee does not anticipate claims 50-53. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Lee therefore are respectfully requested.

V. Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite

Amdt. dated April 2, 2009 - 11 -
Reply to Office Action of January 2, 2009

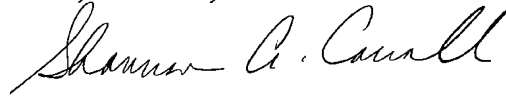
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prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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